## REMARKS

Claims 1, 2, 5, 6, 9 and 13 have been deleted.

Claim 3 has been amended to: delete reference to canceled Claim 1, as well as to esters and prodrugs of the compounds; limit the core members of $R_2$" to those listed on page 5, lines 5 and 6; rearrange the substituents of $R_2$" to clarify which ones may be substituted; limit the number of substituents in each case, as supported on page 5, lines 8, 16 and 24; substitute the meanings of halogen, "lower" in each usage, cycloalkyl, alkoxy, alkenyloxy, alkynyloxy, aryl, $R_x$, carbocyclic aryl, carbocycloalkyl, heterocycloalkyl and heteroaryl, as supported on page 2, lines 15, 21, 25, and 30, page 3, lines 4, 8-10 and 12, and page 4, lines 4 and 5, for clarity; and to make other stylistic and grammatical changes for additional clarity.

Claim 8 has been amended by changing its dependency from canceled Claim 1 to Claim 3, adding the requirement that the composition also comprises a TNF-α release-inhibiting amount of the therapeutic agent according to the instant invention and a diluent or carrier, deleting reference to the use of the compositions to prevention of any disease or condition, and limiting the conditions for which the composition is useful to an inflammatory condition with an autoimmune component, such as arthritis, as supported by page 202, line 3 *et seq*, page 205, lines 5-8 and the assay on page 201, line 8 *et seq*.

Claim 12 has been amended by deletion of a dependency on Claim 1, less-preferred species and spurious terms that clearly had apparently unintentionally appeared in, but did not belong in, this Claim.

Claim 14 has been amended by changing its dependency from Claim 1 to Claim 3, limiting its method to treatments of conditions mediated by TNF-α that are inflammatory conditions comprising an autoimmune component, and

stipulating that the treatment comprises administering a therapeutically-effective *and* TNF-α-inhibiting amount of a therapeutic agent according to the instant invention, and making stylistic and grammatical changes for clarity.

New Claim 15 has been added, representing a narrowing of the scope of the compounds within the composition of Claim 8 to those compounds of Claim 12 or pharmaceutically-acceptable salts thereof.

New Claim 16 has been added, representing a narrowing of the scope of the compounds within the method of Claim 14 to those compounds of Claim 12 or pharmaceutically-acceptable salts thereof.

All deletions have been made without prejudice to Applicants' future rights with respect to the material involved, and as no new matter has been added to any of currently-pending Claims 3, 8, 12 and 14-16, favorable reconsideration of this Application is respectfully requested.

Claims 1-3, 6, 8, 9 and 12-14 have been rejected under 35USC112, first paragraph, over the presence of "ester or prodrug".

Deletion of these terms is believed to fully satisfy and overcome this rejection, as suggested by the Examiner.

Reconsideration and withdrawal of this rejection is respectfully requested.

Claims 6, 8, 13 and 14 have been rejected under 35USC112, first paragraph, over the number of diseases and/or conditions for which Applicants' compounds are useful, and inclusion of "prevention" as a utility for such compounds.

In the interest of expediting allowance of the present Application, Applicants have severely limited the conditions for which pharmaceutical compositions comprising their compounds, and for which methods of treatment comprising use of their compounds, are claimed, and have deleted "prevention" from Claim 8.

Reconsideration and withdrawal of this rejection is, therefore, respectfully requested.

Claims 1-3, 5, 6, 8, 9 and 12-14 have been rejected under 35USC112, second paragraph, over reference to esters or prodrugs in Claim 1, use of "e.g.", "for example", "conveniently" and "including" in Claim 2, the omission of a comma and use of "including" in Claim 3, use of "wherein the R substituents are as defined above" in Claim 5, and inclusion of "Example 91", "Example 161a", "ple 201", and "A solution of toluene-4-sulfonic acid 3-{4-...ester (80 mg, 0.15 mmol), (Step A of Example 190), KCN (20;" in Claim 12.

Deletions of Claims 1, 2, 5, 6, 9 and 13, and amendments to Claims 3, 8, and 12, which, *inter alia*, specifically removed these issues, are believed to fully satisfy and overcome this rejection, and, therefore, its reconsideration and removal is respectfully requested.

Claims 1-3, 5, 6, 8, 9 and 12-14 have been rejected under 35USC103(a) as unpatentable over Adams *et al.*, WO96/40143.

Published International Patent Application WO96/40143 (SmithKlineBeecham Corporation, with J.L.Adams the first named inventor- "the '143 reference") describes 1,4,5-substituted imidazole compounds and compositions containing the substituted imidazole compounds, which include a pharmaceutically-acceptable diluent or carrier, for use as cytokine (particularly IL-1, IL-6, Il-8 or TNF) inhibitors, particularly in cytokine-suppressive, anti-

inflammatory drugs, particularly for treating a CSBP/PK/p38 kinase-mediated disease, as well as various synthetic procedures for producing these imidazole entities.

The '143 reference does not make Applicants' compounds obvious, however, as Applicants' compounds are structurally significantly different from those of the '143 reference and cannot be fairly considered as "structurally analogous" to the compounds with an imidazole group of the '143 reference. Applicants' active compounds with their very different R2" moieties are not disclosed or suggested in any way- and certainly not as between H and $CH_3$ or a $-CH_2$ group, in the reference.

Reconsideration and withdrawal of this rejection is respectfully requested.

Examiner has further noted that Published U.S.Patent Application 2007/0270418 claims subject matter that is substantially similar to that claimed in the instant Application, and, "unless applicants can demonstrate that the instant claims are patentable distinct from the claims of this U.S. Patent [Application], the only way to overcome [this Application] is by way of interference proceedings or removal of the conflicting subject matter".

Accordingly, in the interest of expediting allowance of this Application, Applicants believe they have removed the conflicting subject matter.

## SUMMARY

The Examiner's rejections having been addressed, and the Claims now believed to be in condition for allowance, such favorable action is earnestly solicited, with an early conditional Notice of Allowance being issued. If any remaining matters need to be resolved, however, Applicants respectfully request a telephone interview (the undersigned attorney may be contacted at the

telephone number set forth below) with the Examiner prior to any adverse action being issued by the Office in response to these arguments, in order to facilitate allowance of the pending Claims.

Respectfully submitted,

Dated: March 24, 2009

By 

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